

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all other listings of claims.

1. (CURRENTLY AMENDED) A biocompatible composition useful as an ultrasound contrast agent comprising microbubbles encapsulating a gas within a shell made from intermolecular regions of blended compounds, said compounds comprised of comprising a plurality of polar head groups, each polar head group linked to a straight-chained hydrophobic group(s)] having a chain length different from an adjacent hydrophobic group and sufficient for differing chain lengths, said hydrophobic chains oriented toward the gas phase, whereby the longer chains to lengths assemble beneath the shorter chains thereby enhancing rigidity of stabilizing the shell, the hydrophobic groups oriented toward the gas.

2. (CURRENTLY AMENDED) The composition of Claim 1 wherein the bipolar compounds have the structure:

R₁-X-Z;

R₂-X-Z;

and R₃-X-Z'

where R₁, R₂ and R₃ are hydrophobic groups selected from the group consisting of straight-chained alkyls, alkylethers, alkylthioethers, alkyldisulfides, polyfluoroalkyls, and polyfluoroalkylethers having a carbon chain length greater than or equal to 16 and less than or equal to 32 and where R₁ is greater than R₂ and R₁ is greater than or equal to R₃; R₃ has one or more such hydrophobic groups having the same or different lengths; X is a linker connecting the hydrophobic group to the polar head group; Z is a polar head group selected from the group consisting of CO₂M⁺, SO₃M⁺, SO₄M⁺, PO₃M⁺, PO₄M⁺₂, N(R)_n⁺, a pyridinium or substituted pyridinium group, and a zwitterionic group; R is selected from the group consisting of -H, -CH₃, alkyl, cycloalkyl, substituted cycloalkyls containing one or more heteroatoms, and benzyl and can be the same or different; and Z' is a nonionic group.

3. (PREVIOUSLY PRESENTED) The composition of Claim 2 wherein R₁, R₂ and R₃ are straight-chained alkyl groups having from about 20 to 30 carbon atoms.

4. (PREVIOUSLY PRESENTED) The composition of Claim 2 wherein X is selected from the group consisting of -(CH₂)_m-, -(CH₂)_mCO₂(CH₂)_n-, -(CH₂)_mCONH(CH₂)_n-, -(CH₂)_mNHCONH(CH₂)_n-,

$-(CH_2)_mOCONH(CH_2)_n$, $-(CH_2)_mO(CH_2)_n$, $-(CH_2)_mNH(CH_2)_n$, $-(CH_2)_mN[(CH_2)_n]_2$,
 $-(CH_2)_mS(CH_2)_n$, $-(CH_2)_mSO(CH_2)_n$, $-(CH_2)_mSO_2(CH_2)_n$, $-(CH_2)_mNH(CH_2)_nCO_2(CH_2)_o$,
-[(CH_2)_m]₂N(CH₂)_nCONH(CH₂)_o-, where m, n, and o are the same or different and are less than 5,
DL-lysine, aspartic acid, glutamic acid, serine, cysteine, homocysteine, cystine, serinol, itaconic
acid, tiglic acid, maleic acid, DL-malic acid, succinic acid, tartaric acid, malonic acid, citric acid,
phthalic acid, terephthalic acid, N,N-bis[2-hydroxyethyl]-2-aminoethanesulfonic acid, N,N-bis(2-
hydroxyethyl)glycine, 3-[N,N-bis(2-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, N-
tris[hydroxymethyl]methyl-3-aminopropanesulfonic acid, and N-tris[hydroxymethyl]glycine.

5. (CURRENTLY AMENDED) The composition of Claim 2 wherein Z' is selected from the group consisting of polysorbates, polyglycerols, polypeptides, polynucleotides, polysaccharides, polyvinylpyrrolidones, polyvinylalcohols, polyethyleneglycols, and composites combinations thereof.

6. (PREVIOUSLY PRESENTED) The composition of Claim 2 wherein Z' is poly(ethyleneglycol) with the number of ethyleneglycol monomer units greater than or equal to 20.

7. (CURRENTLY AMENDED) A method for obtaining an ultrasound contrast image of body tissue comprising:

administering into a body a biocompatible composition useful as an ultrasound contrast agent comprising microbubbles encapsulating a gas within a shell made from intermolecular regions of blended compounds, said compounds comprised of comprising a plurality of polar head groups, each polar head group linked to a straight-chained hydrophobic group[s] having a chain length different from an adjacent hydrophobic group and sufficient for differing chain lengths said hydrophobic chains oriented toward the gas phase, whereby the longer chains to lengths assemble beneath the shorter chains thereby enhancing rigidity of stabilizing the shell, the hydrophobic groups oriented toward the gas, and

taking an ultrasound image of the desired tissue.

8. (CURRENTLY AMENDED) The method of Claim 7 wherein the bipolar compounds have the structure:

R₁-X-Z;
R₂-X-Z;

and $R_3\text{-}X\text{-}Z'$

where R_1 , R_2 and R_3 are hydrophobic groups selected from the group consisting of straight-chained alkyls, alkylethers, alkylthioethers, alkyl/disulfides, polyfluoroalkyls, and polyfluoroalkylethers having a carbon chain length greater than or equal to 16 and less than or equal to 32 and where R_1 is greater than R_2 and R_1 is greater than or equal to R_3 ; R_3 has one or more such hydrophobic groups having the same or different lengths; X is a linker connecting the hydrophobic group to the polar head group; Z is a polar head group selected from the group consisting of $\text{CO}_2\text{-M}^+$, $\text{SO}_3\text{-M}^+$, $\text{SO}_4\text{-M}^+$, $\text{PO}_3\text{-M}^+$, $\text{PO}_4\text{-M}^+$, $\text{N}(\text{R})_4^+$, a pyridinium or substituted pyridinium group, and a zwitterionic group; R is selected from the group consisting of $-\text{H}$, $-\text{CH}_3$, alkyl, cycloalkyl, substituted cycloalkyls containing one or more heteroatoms, and benzyl and can be the same or different; and Z' is a nonionic group.

9. (PREVIOUSLY PRESENTED) The method of Claim 8 wherein R_1 , R_2 and R_3 are straight-chained alkyl groups having from about 20 to 30 carbon atoms.

10. (PREVIOUSLY PRESENTED) The method of Claim 8 wherein X is selected from the group consisting of $-(\text{CH}_2)_m\text{-}$, $-(\text{CH}_2)_m\text{CO}_2(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{CONH}(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{NHCONH}(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{OCONH}(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{O}(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{NH}(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{N}[(\text{CH}_2)_m]_2\text{-}$, $-(\text{CH}_2)_m\text{S}(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{-}$, $-(\text{CH}_2)_m\text{SO}(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{SO}_2(\text{CH}_2)_n\text{-}$, $-(\text{CH}_2)_m\text{NH}(\text{CH}_2)_n\text{CO}_2(\text{CH}_2)_o\text{-}$, $[(\text{CH}_2)_m]_2\text{N}(\text{CH}_2)_n\text{CONH}(\text{CH}_2)_o\text{-}$, where m , n , and o are the same or different and are less than 5, DL-lysine, aspartic acid, glutamic acid, serine, cysteine, homocysteine, cystine, serinol, itaconic acid, tiglic acid, maleic acid, DL-malic acid, succinic acid, tartaric acid, malonic acid, citric acid, phthalic acid, terephthalic acid, N,N-bis[2-hydroxyethyl]-2-aminoethanesulfonic acid, N,N-bis(2-hydroxyethyl)glycine, 3-[N,N-bis(2-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, N-tris[hydroxymethyl]methyl-3-aminopropanesulfonic acid, and N-tris[hydroxymethyl]glycine.

11. (CURRENTLY AMENDED) The method of Claim 8 wherein Z' is selected from the group consisting of polysorbates, polyglycerols, polypeptides, polynucleotides, polysaccharides, polyvinylpyrrolidones, polyvinylalcohols, polyethyleneglycols, and ~~composites~~ combinations thereof.

12. (PREVIOUSLY PRESENTED) The method of Claim 8 wherein Z' is poly(ethyleneglycol) with the number of ethyleneglycol monomer units greater than or equal to 20.

13. (PREVIOUSLY PRESENTED) The method of Claim 7 wherein the tissue is the heart and the image is a myocardial perfusion image.

14. (WITHDRAWN) A method for measuring pressure or fluid flow rates in a closed system comprising:

inserting a composition useful for measuring pressure or fluid flow rates comprising microbubbles encapsulating a gas within a shell made from a blend of bipolar compounds having inter-molecular hydrophobic regions of mixed carbon chain length into a closed system;

measuring the acoustic changes with frequency for the system; and
calculating the change in pressure or change in fluid flow rate.

15. (WITHDRAWN) The method of Claim 14 wherein the bipolar compounds have the structure:

R₁-X-Z;

R₂-X-Z;

and R₃-X-Z'

where R₁, R₂ and R₃ are hydrophobic groups selected from the group consisting of straight-chained alkyls, alkylethers, alkylthioethers, alkyldisulfides, polyfluoroalkyls, and polyfluoroalkylethers having a carbon chain length greater than or equal to 16 and less than or equal to 32 and where R₁ is greater than R₂ and R₁ is greater than or equal to R₃; R₃ has one or more such hydrophobic groups having the same or different lengths; X is a linker connecting the hydrophobic group to the polar head group; Z is a polar head group selected from the group consisting of CO₂M⁺, SO₃M⁺, SO₄M⁺, PO₃M⁺, PO₄M⁺, N(R)₄⁺, a pyridinium or substituted pyridinium group, and a zwitterionic group; R is selected from the group consisting of -H, -CH₃, alkyl, cycloalkyl, substituted cycloalkyls containing one or more heteroatoms, and benzyl and can be the same or different; and Z' is a nonionic group.

16. (WITHDRAWN) The method of Claim 15 wherein R₁, R₂ and R₃ are straight-chained alkyl groups having from about 20 to 30 carbon atoms.

17. (WITHDRAWN) The method of Claim 15 wherein X is selected from the group consisting of -(CH₂)_m-, -(CH₂)_mCO₂(CH₂)_n-, -(CH₂)_mCONH(CH₂)_n-, -(CH₂)_mNHCONH(CH₂)_n-, -(CH₂)_mOCONH(CH₂)_n-, -(CH₂)_mO(CH₂)_n-, -(CH₂)_mNH(CH₂)_n-, -(CH₂)_mN[(CH₂)_m]₂-, -(CH₂)_mS(CH₂)_n-, -(CH₂)_m-, -(CH₂)_mSO(CH₂)_n-, -(CH₂)_mSO₂(CH₂)_n-, -(CH₂)_mNH(CH₂)_nCO₂(CH₂)_n-, -[(CH₂)_m]₂N(CH₂)_nCONH(CH₂)_n-, where m, n, and o are the same or different and are less than 5,

DL-lysine, aspartic acid, glutamic acid, serine, cysteine, homocysteine, cystine, serinol, itaconic acid, tiglic acid, maleic acid, DL-malic acid, succinic acid, tartaric acid, malonic acid, citric acid, phthalic acid, terephthalic acid, N,N-bis[2-hydroxyethyl]-2-aminoethanesulfonic acid, N,N-bis(2-hydroxyethyl)glycine, 3-[N,N-bis(2-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, N-tris[hydroxymethyl]methyl-3-aminopropanesulfonic acid, and N-tris[hydroxymethyl]glycine

18. (WITHDRAWN) The method of Claim 15 wherein Z' is selected from the group consisting of polysorbates, polyglycerols, polypeptides, polynucleotides, polysaccharides, polyvinylpyrrolidones, polyvinylalcohols, polyethyleneglycols, and composites thereof.
19. (WITHDRAWN) The method of Claim 15 wherein Z' is poly(ethyleneglycol) with the number of ethyleneglycol monomer units greater than or equal to 20.
20. (WITHDRAWN) The method of Claim 14 wherein the closed system is the body circulatory system